Biochemistry
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Lecture - 15
Nucleic Acids III

In the last two classes we spoke about lipids and membranes. Now, what we are going to consider today is how we have the transport from the inside of the cell to the vice versa. So a specifically membrane transport that we going to talk about today.

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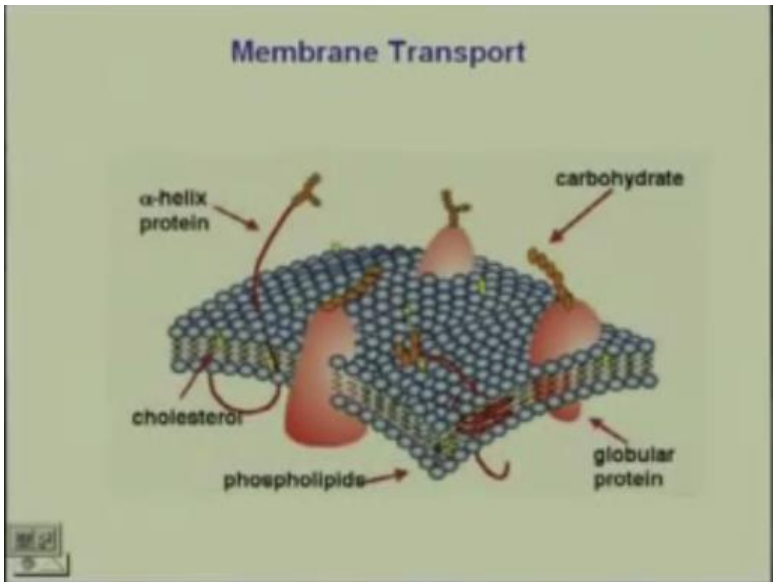

Now, if we look at the fluid mosaic model that we discussed in the last class, we know that is lipid bilayer that comprises the membrane is intercept with proteins and channels that allow the transport of ions from one side to the other, whether it is from the inside to the outside or from the outside to inside of the cell. Now this is extremely important for cellular process that are going on, and you also realize all types of molecules will not be transported into the cell.

Not only because of their size but also because of the polarity because the lipid bilayer has a polar head group on either ends but it is intercept this hydrophobic tails of the lipid. Now because it is intercept by the hydrophobic tails of the lipid we have specific proteins that are going to allow the transfer of ions and molecules.

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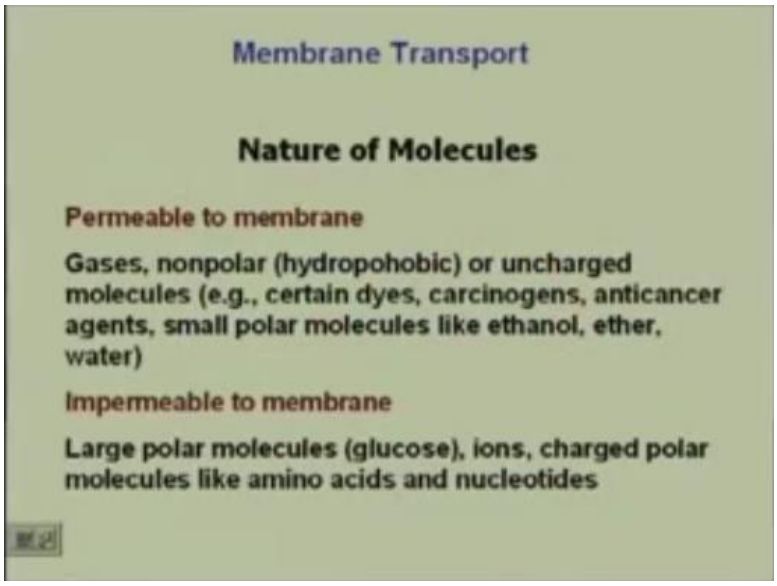

But before we were go into that we will see the nature of molecules that are going to be transported. First of all, we consider those set of permeable to the membrane and those that are impermeable to the membrane. For example, if we look at small non-polar hydrophobic, uncharged molecules, small polar molecules, gases, these will be permeable to the membrane. Because they would generally, basically diffuse through the membrane.

But, if we look at other molecules, larger polar molecules for example, ions or charged polar molecules like amino acids, a nucleotide for example, adenosine monophosphate(AMP), ADP, or ATP. Now these would be impermeable to the membrane because as I mentioned that since we have this hydrophobic lipid layer it is unlikely that is going to allow a charged molecule to pass through. So you have to have some channel or some way that the molecule has to get through.

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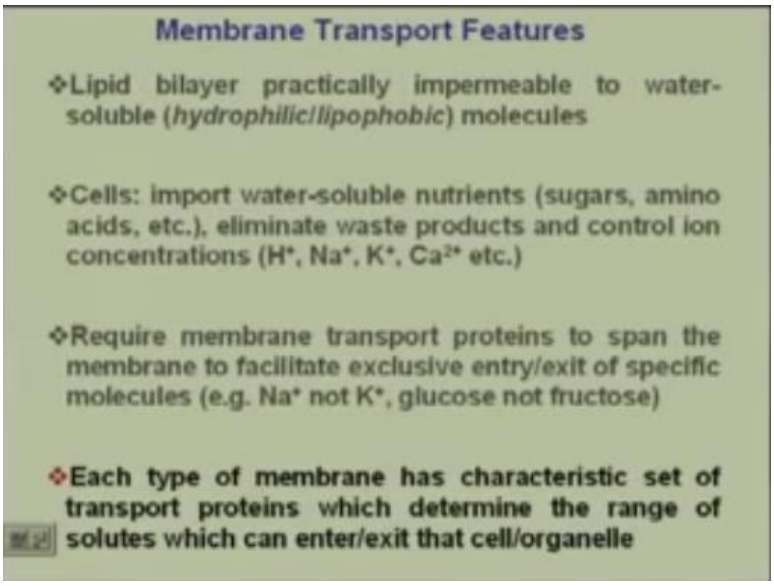

So, considering what could happen, let us see what the transport some of these futures are. First the lipid bilayer practically impermeable to water-soluble that is hydrophilic molecule, the reason again being because it is a lipid bilayer. It would not allow this transfer to be favorable. Second, cells - what cells actually do is, they important water-soluble nutrients, like sugar, amino acids; they eliminate waste products and control ion concentrations.

Now this is extremely important in maintaining what is called a sodium-potassium balance in our cells. So this is what cells actually have to do and to do this in the importing of the water-soluble nutrients or the elimination of the waste products that has to be done through these channels. So what you have to have is we have as we have studied we have integral membrane proteins, we have peripheral membrane proteins and we have anchor proteins.

So what happens is there is a specific requirement for membrane transport proteins that have to span the membrane to facilitate exclusive entry or exists of specific molecules, okay for the specific transfer or for the specific action of the cells there are these specific transport proteins and because each of them have a specific molecule that they are going to bind and transport each membrane transport activity is unique.

Now each type of membrane therefore, has a characteristic set of transport for proteins which will determine what is going to enter the cell, it is like a security control. Each of these

membrane proteins will exactly determine what type of ions or molecules are going to enter the cell and when they are going to enter the cell all this is controlled by these transport proteins.

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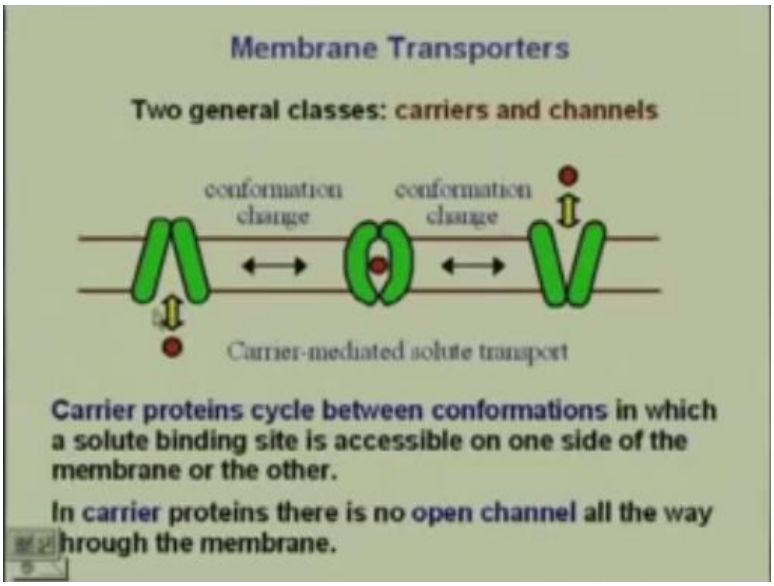

Now, the membrane transporters that are these proteins are actually of two general classes. The two general classes are carriers and channels, okay. Now that carriers do is actually, in a carrier-mediated solute transport because of the lipid bilayer, it is unlikely that you, this specific solute will be allowed to go from one side of the membrane to the other, solely because of the lipid hydrophobic tails that are present here.

So what happens is there is a specific carrier protein that cycle between conformation which allow the solute binding on one side and release on the other side. Okay, so what actually happens is there is a specific conformational change that occurs bringing it into a fashion that will allow and opening on one end of the membrane only. So it is not a channel. A channel is something that would be through, all through.

So this is what you would call a carrier protein, this i.e. carries a molecule from one side to the other. And in doing this it has to have a conformational change that occurs only on the legend binding. So once the legend is bound what happens is, it changes its conformation, then it sorts of a reaction is instigated where the molecule is then eliminated on the other side of the

membrane. Then, to come back to this it probably takes in the waste molecules from the cell, and then changes its conformation again then goes back to where it is started from.

Exactly like a normal enzymatic mechanism. You know that it goes through a certain mechanism where there is a certain change, and then to revert back it has to just do the opposite of what it had done. Okay, so this is how a carrier protein would cycle between conformations in which the solute binding would be accessible on one side of the membrane or the other and there is no open channel all the way through the membrane.

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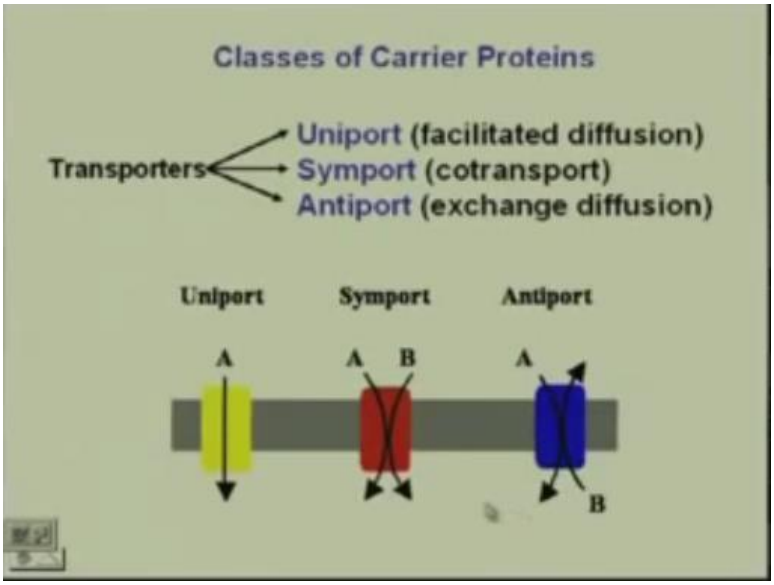

Now these can be of different types. They can be what is called Uniport, Symport or Antiport. Okay now what this means is you have -- I can show you the diagram here it will be easier. In a Uniport transporter, you have facilitated diffusion that takes. So A is going, so it is going from one direction to the other, that's Uniport it has just one directional movement. Symport has bi-directional movement.

Okay so it is co-transported, it transports A and B together. So it is a synchronies process that occurs when you have a Symport. In Antiport, you have in an exchange diffusion. You have A going in one direction and B going in the opposite direction, okay. So the classes of carrier proteins these transporters are either Uniport, Symport or Antiport and Uniport means that you have just the transfer of one set.

Symport means you have the simultaneous co-transport of A and B together. And Antiport means you have exchange diffusion where A is going in one direction and B in the opposite direction.

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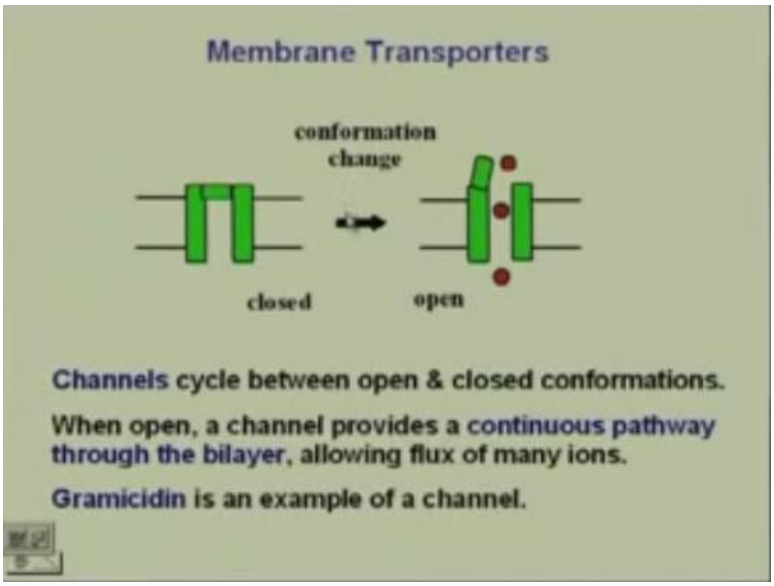

Now, we look at ion channels. Now the ion channels are we have basically openings through openings. But, these are also sometime what are called 'Gated ion channel'. Gated means, basically it has a gate. Okay. So it opens and closes depending on concentration differences inside the cell and outside the cell. So whether a cell means potassium or sodium would depend upon whether this ion channel is going to open or close. Okay.

So the channels basically cycle between open and closed conformations. And when open, you recognize it is not like a carrier protein, where a carrier protein does not allow anything else to get through. Once this channel is open, there is going to be a flux of many ions going through because you have an open channel now, okay. So this channel is actually very sensitive to the flux.

So what is going to happen is as soon as there is too many going through it just like a security gate. As soon as it sees too many ions going through it just shuts itself, okay. This is unlike the carrier protein where you recognize that once the legend is bound then what happens is there is a

conformational change, but nothing else can get through. But, when we have this open channel it forms a continuous partly through the bilayer.

So it is open for everybody to get through. Okay, so all the ions will just try and push themselves through, but the cell might not require those ions, so then it will shut the gate, so nothing is not allowed through it; it is a beautiful way that these membranes actually work. And Gramicidin is an example of such an ion channel, the structure of which was solved quite a few years ago which is a combination actually of D and L amino acids.

This is one of the proteins that not only has L amino acid but also has D amino acids. So what we saw – find is a conformational change in this case also but the cycling is between an open and closed conformation. So the differences between what you would have a carrier protein and an ion channel is quite clear here, right.

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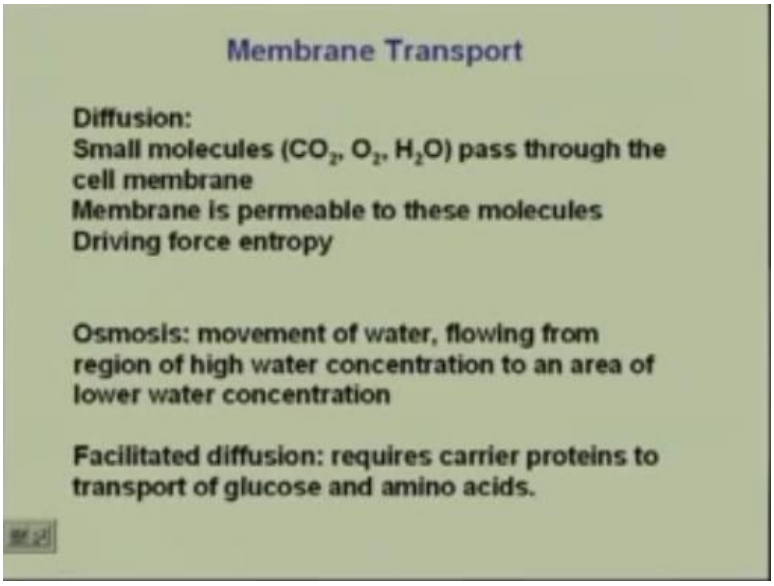

Okay. Now how does this transport take place? They can be diffusion. Okay. They can be Osmosis. They can be what is called Facilitated diffusion, okay. Let us go one by one. When we consider diffusion, it is just like small molecules that pass through the cell membrane. Okay, just generally pass through because there is just enough interstitial space or (()) (11:25) but you see that none of these are charged in this sense.

So they just pass through the cell and the membrane is basically permeable to these molecules. So it just an ordinary diffusion. Now you recognize if this is essential so that you have the CO_2, O2 because when you have oxygen bound to hemoglobin, right or the CO_2 bound that has to be released, it has to be a normal diffusion in and out of the cell. Osmosis, will allow the movement of water.

Following from a region of high water concentration to a region of low water concentration. And I am sure all of you know what osmosis is. Facilitated diffusion is something that carrier proteins do. What they do? Is they help the diffusion of the certain proteins or certain ions or glucose or amino acids or whatever has to go through the membrane it helps, so it is a diffusion but it is helped or facilitated by the presence of a carrier proteins. Okay, so we have diffusion, we have osmosis; we have facilitated diffusion.

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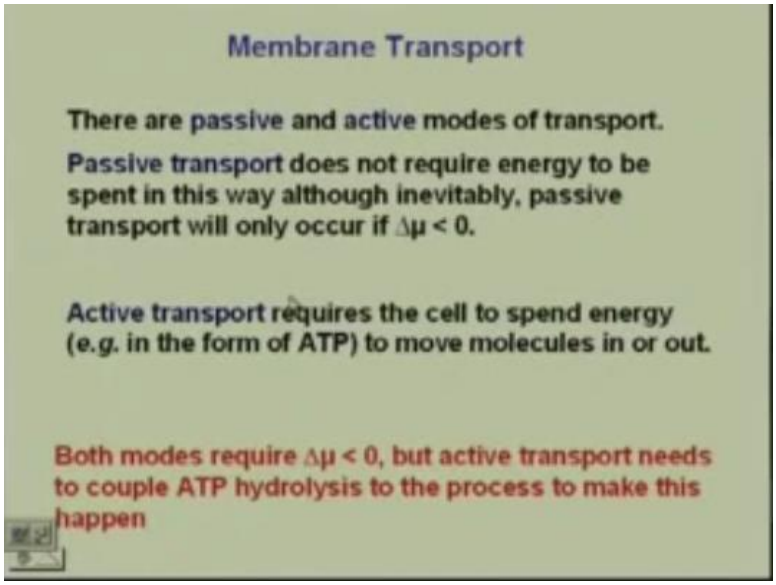

We also have two other kinds of transport that are called Passive and Active modes of transport. Okay. Now, when we have passive transport, it means that there is no extra energy required for the transport of the solute from one end to the other. Now, when we speaking of energy, okay. We are speaking of the free energy, so it is a spontaneous movement of the solute molecules from one side to the other be it inside to outside or outside to inside. That is what is called passive transport.

When you have active transport, it means you are going against a gradient, okay. If you are going against the gradient you have to push your way through. And in pushing your way through you have to expand energy, okay. That energy comes from ATP hydrolysis. It is coupled with – we will understand ATP hydrolysis and where this energy is all coming from when we do bioenergetics.

But for now, we have to know that when we have this membrane transport we have two kinds of transport where we have passive transport that does not required any energy for the solute molecules to pass through and active transport where the cell has to spend energy and the place where it gets energy from is from ATP hydrolysis.

ATP hydrolysis there is a high energy born that breaks and energy is produced and it is beautiful in the way that there are two reactions that are always couple together where one reaction needs the energy and ATP supplies that energy, it is not that ATP will just breakup to provide the energy if it is not require.

So essentially for both cases you understand that this Delta Mu that is a free energy change has to be less than 0 because it has to be a process where the spontaneous transport of a solute molecules is going to occur, okay. In the case of passive transport, this extra energy is not required so Delta Mu is less than 0. But for the active transport, where one of the reactions is going to have a delta G that is positive.

The energy released from ATP is going to more than compensate for that Delta G positive value and give you an overall delta G that is negative and this will be coupled therefore. So the two reactions will be coupled to give you an overall delta G that is negative, so that the transport can occur.

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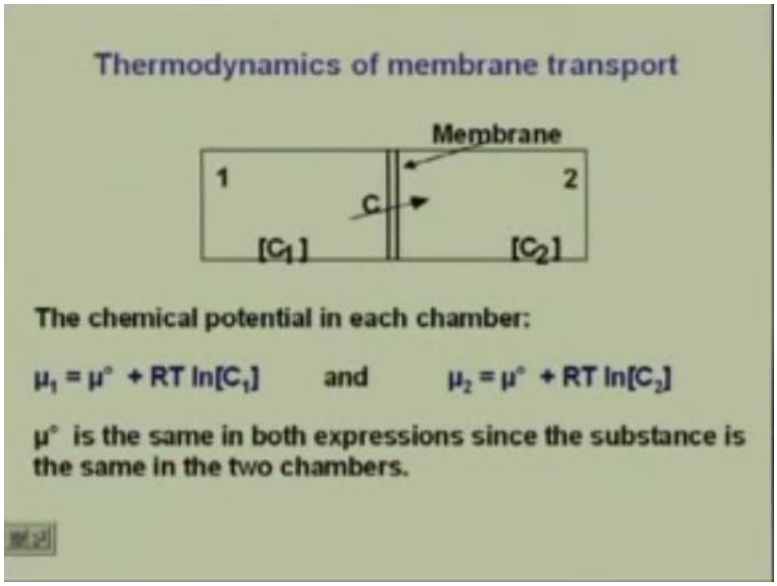

Okay, now if we look at the Thermodynamics of membrane transport, we speaking about free energy and how this all can occur. Okay so basically we are looking at two chambers here, where we are transporting one solute say or one substance from one side to the other, okay.

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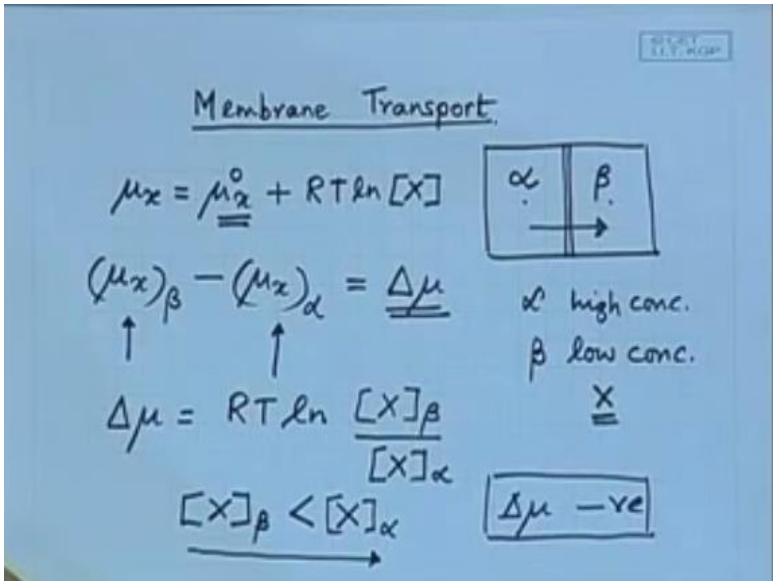

Now if we look at this generally we have say just general membrane transport where we looking at say a box here where we have a membrane and we are looking at a region say alpha going to beta. Alpha is a region of high concentration and beta is region of low concentration of say a solute X. So now when we write the chemical potential, we have new X, which equal to new 0x+RT ln [x] in general. Okay.

Okay now we have this going from A to B then we have to look at the change of new X B because that is our final state minus new X alpha which is our initial state. That is going to give our Delta Mu, okay. So if we write out this for beta and we write out this for alpha, the Delta Mu that this is associated with this is going to be RT ln because what happens is this cancels out; because we are speaking about the same solute X.

So we have RT ln the concentration of X in, the beta low concentration side and the concentration of X in the alpha side. Now we know that the concentration of X at the beta side is less than the concentration of X on the alpha side. So what can I say about Delta Mu? It is negative. Okay. So what do I have here, I have a spontaneous process that is going to allow the transport of X, from the high concentration side to the low concentration side.

Okay this is something you have done before. But it is just basic thermodynamic that all of you have studied. But what we are looking at is we are looking at the normal spontaneous reaction that is going to occur here because Delta Mu is negative and we have the transport of X going from alpha to beta, where alpha - where the concentration of X in alpha is at the high concentration and at the low concentration.

So this is similar to what we have here, where we are considering the concentration of component C and we have again the chemical potential calculations, where we can than determine what the transfer Delta Mu is going to be from 1 to 2, so it is going to be Mu2 – Mu1 again we have RT ln C2 by C1, and if you put in the current value of R you are going to get here Delta G value in joules or kilojoules per mole.

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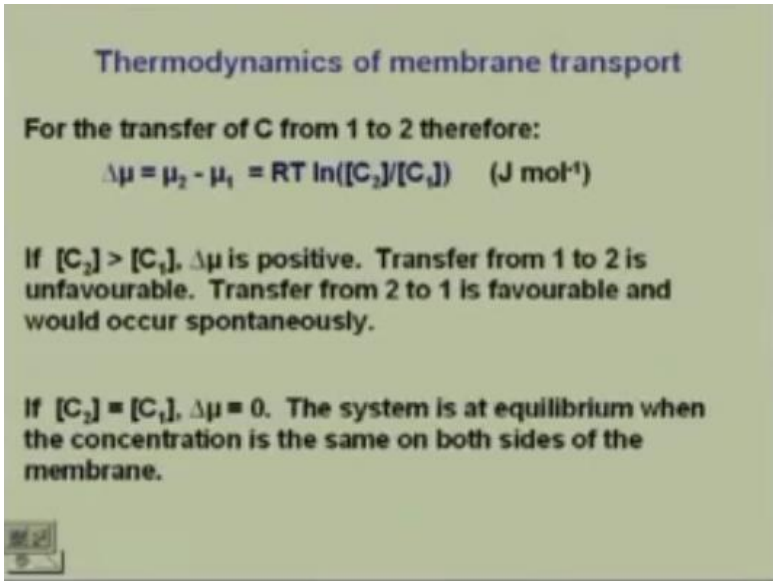

Now if the concentration of C2 is higher, then this is going to be positive. If the concentration of C2 is higher than C1 then we have a positive value for ln which makes Delta Mu positive. So the transfer from 1 to 2 is going to be unfavorable, right. So what do I have to do in that case if I have to have the transfer occur in terms of a membrane transport, I have to couple it with ATP hydrolysis?

ATP hydrolysis is going to give me a huge amount of energy that is going to compensate for the positive amount that I get here. Okay we will see that very clearly when we do Bioenergetics. But for now what we need to know is for the transfer, if I have this C2 greater than C1 then my delta new is positive so the transfer is not going to be favorable. However, if C2 is less than C1 then my ln is negative and my Delta Mu is negative, so the transfer of 2 to 1 would occur spontaneously because I have a negative.

And then when do I have equilibrium? When I have the same concentration on both sides. But this does not happen in membrane transport. You do not have continuous diffusion till the levels of the concentration are the same on both sides. For example, we will be considering the sodium and potassium levels in the cell which are -- they never get to a constant level, if they do you will be seriously in trouble with your health.

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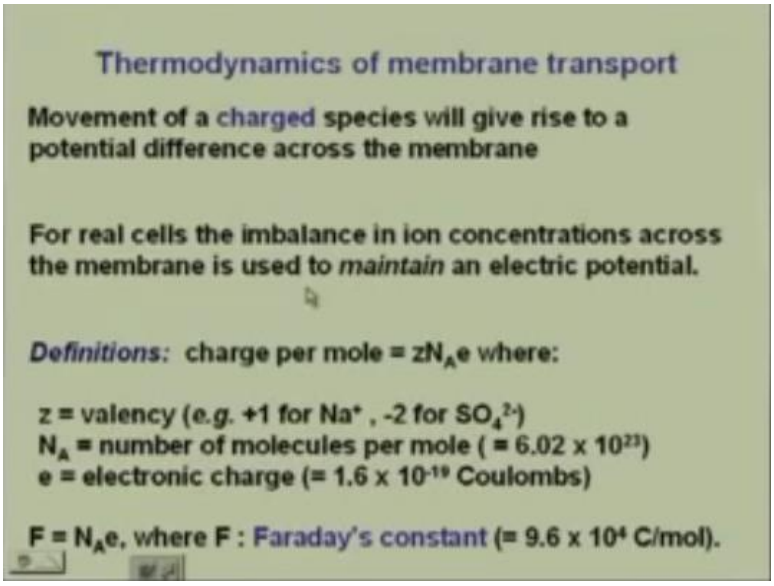

Okay. So let us consider what we have here. Now when I speak about the sodium-potassium channel or a sodium-potassium transport, you understand that it is transporting ions now. Now when I transport ions, I do not have a free energy only associated with the transport due to the chemical potential, not only a concentration difference, I also have an electrochemical potential associated with it. Okay. So what do I have, the free energy change is going to be associated –

You know Delta G; Delta G has with an electrochemical potential you have it equal to -nfe. So not only do you have the potential due to the concentration difference, you also have a potential due to the electrochemical difference when you are transporting ions, okay. So when we have the movement of these charged species it will give a rise to the potential difference across the membrane, right.

Now due to the potential difference rise, there is going to be an imbalance of ion concentrations across the membrane, okay. So we have to have an electric potential. Now we know, now this is just a basic definition's which you all know. You have a z. What is a z? z is a valency. You have N_A which is Avogadro's number and you have e which is the electronic charge, okay. And we have this F, what is F, F is Faraday's constant that is Avogadro's number into the electronic charge.

Okay so basically what – what we are saying now is when I do not have just a concentration difference but I also have the transport of a charged species I have to consider an additional electrochemical potential. So what do we do now?

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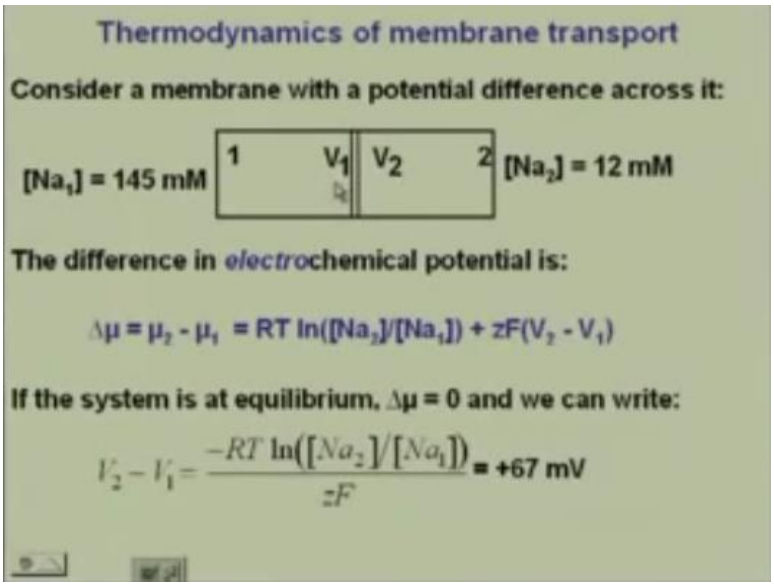

So we have a membrane with a potential difference across it. Now, I not only have, if you look at this expression here, what is this expression have? It has an associated with it a concentration because of the difference in the levels of concentration of sodium and -- a sodium in side 1 and side 2. But, since we have charged species now, what do I have? In addition, I have an electrochemical potential.

And this also going to contribute to my Delta Mu, okay. So I have now, a system where at N_a1 say, this is the concentration of the sodium at side 1, it is a 145 millimolar. The concentration at side 2 is 12 millimolar. Now, when I consider the Delta Mu, I also have to consider, so where am I, I am transferring from 1 to 2, right. So let us go back to this just to make it clearer.

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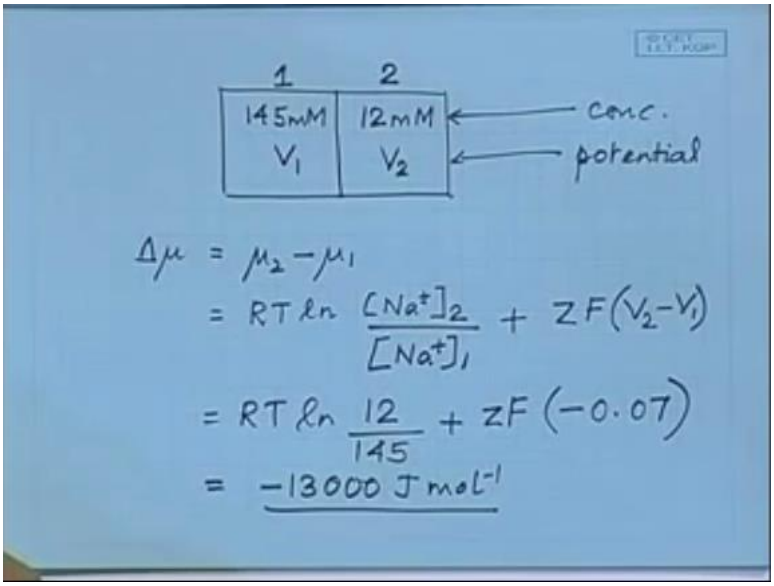

So I have now, let us say I have my cell and here, I have chamber 1 and here I have chamber 2. In chamber one, I have the concentration at 145millimolar for sodium and the potential V1. In chamber two, I have 12 millimolar in V2 which is the potential. So if I am to calculate the Delta Mu value I have to consider Mu2 – Mu1, so the contribution is going to come from RT ln, what it is going to be?

[Na+]2. Because that is our final state. [Na+]1. Also, I have ZF (V2-V1), the delta V that I have. So if I calculate this actually, I am going to have, what is this? It is 12/145 both are in millimolar and I have a Z and an F and this V2-V1 is actually 70 millivolts, minus 70 millivolts, so we have this. Okay. Now if I calculate this it works out to be -13000 J moL-1. So what it is saying? That the transport of sodium from this higher concentration side to the lower concentration side is a favorable process.

And you have a process that is a concentration that you have to consider and the potential that you have to consider. So these are the two considerations that you have to make when you are transporting a charged species through the membrane.

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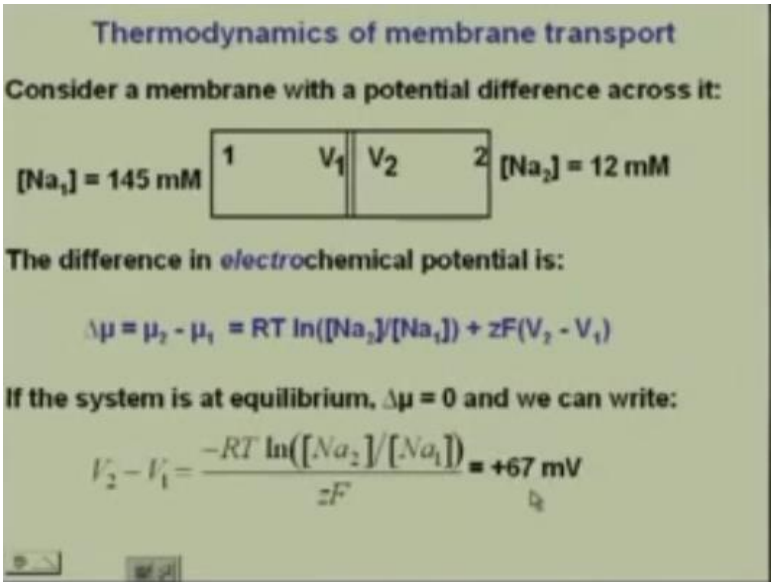

So what we have, is we have a Delta Mu that is Mu2-Mu1, RT ln([Na2]/[Na1]) that is the concentration of ions on the both sides plus $_{Z}$F(V2-V1). When the system is at equilibrium we can write this which turns out that this V2-V1 is 67 millivolts.

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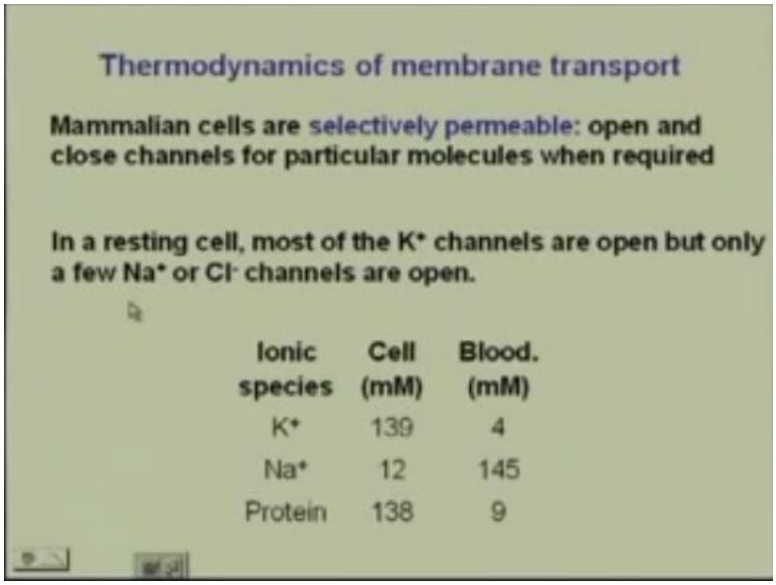

Now, this is very important. When we consider the ionic species in the cell, the concentration in the cell and the concentration in the tissue or in the blood, if you notice the concentration of potassium in the cell is high, and the concentration of sodium is low.

In the blood, it is just the opposite. Now this is the extremely delicate balance, you can have severe brain damage if this balance is even slightly distorted, okay. If your sodium level in the

blood goes -- even if you say potassium level goes down to 3 millimolar and your sodium level goes down to 120 millimolar, you will have to be administered saline to get and the given potassium chloride to get your levels backup.

And you cannot do that very drastically because your brain will be irreversibly damaged. It is extremely delegated. So even this 4 millimolar cannot go down to 3 millimolar. This cannot even go down to a 120 millimolar. Okay, it is that delicate balance and this is extremely important because we have a specific carrier protein that act on sodium and potassium. So what it does is it brings the sodium out of the cell and if there is a same protein that will take the extracellular potassium into the cell.

It is quiet smartly, very, very smartly designed. So if we consider this Mammalian cells they are selectively permeable and they open and close channels for particular molecules when they are required as I mentioned before, because you cannot have too much sodium in the cell. You cannot have too much potassium also. Too much is also bad. Okay. Now in a resting cell, most of the potassium channels are open. Why?

Because, it can have a large amount of potassium in the cell not outside. So what do we have to have here? We have to have an ion gated channel, okay. The ion gated channel will -- in this case what happens for the resting cell, most of the potassium channels are open so that the potassium ions can come through but only a few of the sodium channels are open, because we don’t want too much sodium in the cell.

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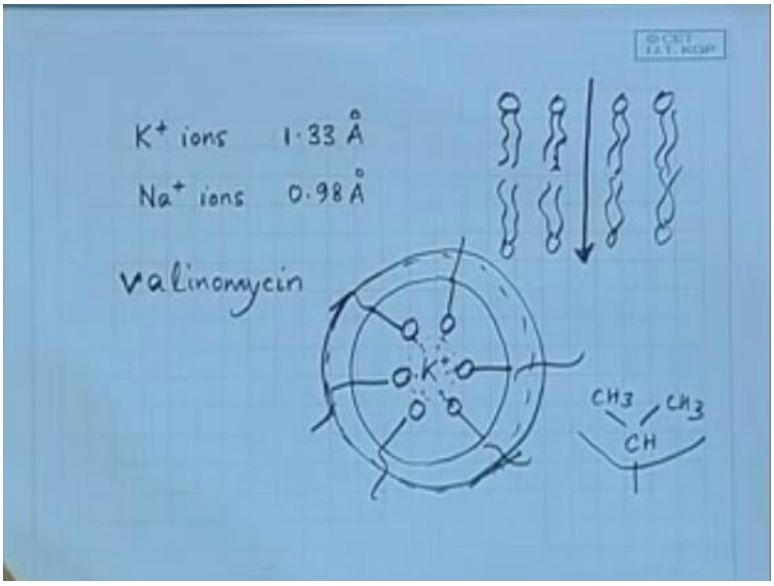

Now if we look at some interesting futures of the sodium and potassium ions then what we have here is if we look at the radius sodium and potassium ions, we have K+ ions, that has a radius of 1.33 Angstroms. We have Na+ ions that have a radius of 0.98 Angstroms. Okay. Now if we consider that the sodium's ions are small. So it is likely that they are going to go through more easily. But that is not true.

You know that when you have hydration, right. The hydration sphere is different for sodium and potassium. But when it enters the cells it is strips of the hydrations sphere. Because what you have to do is you now have to traverse this membrane. Now there is a certain molecule that is very cleverly designed called valinomycin. It is valinomycin. This is under circular molecular it is made up of six amino acids.

So we have some amino acid chains, that's -- valinomycin means there are valine amino acid, valine side chain rather that are outside here. So what are the valine side chains? What is the valine side chain? It is CH – CH3 – CH3. What type of a group is it? A hydrophobic group. So, here we have a hydrophobic shell. Now this hydrophobic shell in here has six oxygen atoms. Okay. Now these six oxygen atoms are spaced in such a way that this fits the potassium ion exactly.

And because of this hydrophobic surface that you have, what happens? It can pass through the membrane very easily, right. So the size is such that the interaction between the oxygen and the potassium charge -- charges, the ionic interaction is unique. Now because sodium is too small it does not sit here. It does not have the specific interaction that potassium has. So it is not transferred as efficiently. Okay.

Now this is useful because the concentration on K+ shell has to be high. Okay. So the fact that valinomycin actually binds K+ with the much, much higher affinity than sodium is useful for the transfer of the potassium ion in the cell. Okay. So and the reason for having these specific amino acids, hydrophobic type of amino acids on the surface is so that it can just pass through the lipid bilayer, okay. So it can interact with these lipid hydrophobic tails and pass through.

So nature has designed everything. So what we have here? Is we have in a resting cell the K+ channels open, where it is transported using this valinomycin also but few of the sodium channels open.

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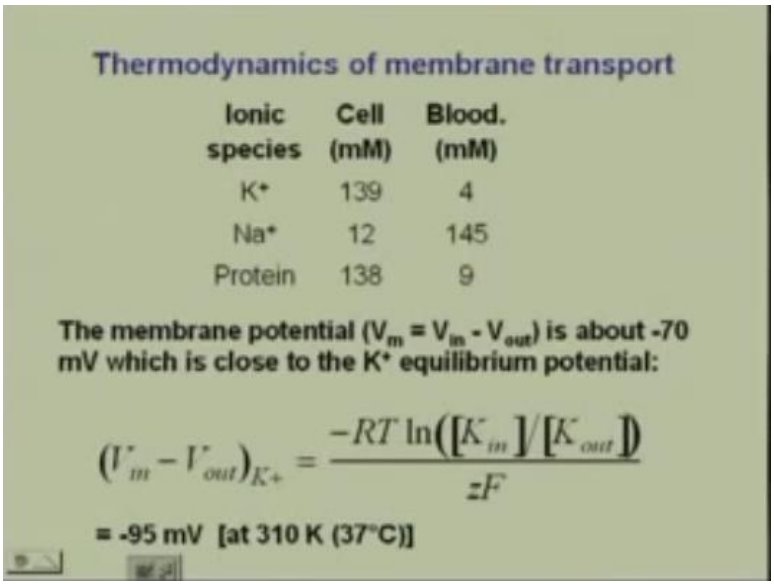

Now the membrane potential which I used in the expression that I used before for the sodium potassium where we have -17 millivolts which is why we calculated the Delta Mu**.** We calculated to the -13000 joules per mole. Okay. So what was that due to, that was due to the sodium

concentration and also the potential difference. What is this potential? It is a membrane potential we are talking about.

Why do we have a membrane potential? Because we have different amounts of charged species on either side of the membrane, so that is going to give rise to a membrane potential, it is also going to give rise to a concentration gradient. And in the calculation of the Delta G. We have to utilize not only the concentration gradient, but also the membrane potential. And later on, when we study about ATP hydrolysis and the ATPase pump. We will have what is called a proton gradient.

So not only are we going to have a concentration change, we are going to have a concentration change, a membrane potential and also a proton concentration gradient which is going to give rise to a PH gradient. Okay, now that is also an important. Okay, so we are going to have when the Delta G contributions will be from three levels: concentration, membrane potential and PH. Okay. We will do that later when we consider ATP transfer.

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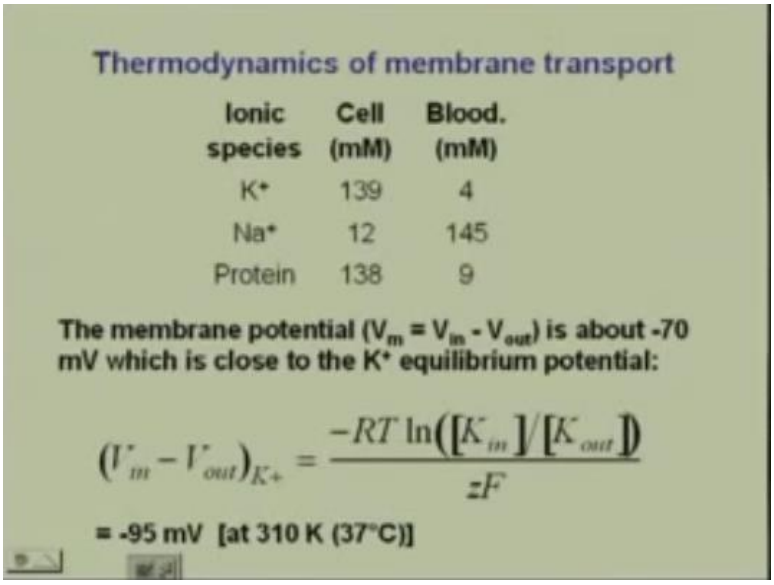

So now this is what we have for the potassium. We work it out for the sodium, this is what we have for the potassium for the sodium it came out to the 67 millivolts, here it is -95 millivolts at 310K at a 37 degree centigrade which is normally where you would do earlier biological calculation. The PH 7.4, and 37 degrees centigrade which in some books in most of the books in

-where you will read biochemistry, the Delta G 0 has a prime to it. The Delta G 0 prime means that, that was a biological standard. Okay.

In the normal Delta G 0 what do you consider? 298 Kelvin. When it is the prime it means it is 37 degree centigrade that's 310 Kelvin and the PH is 7.4. Okay, that is what that prime means.

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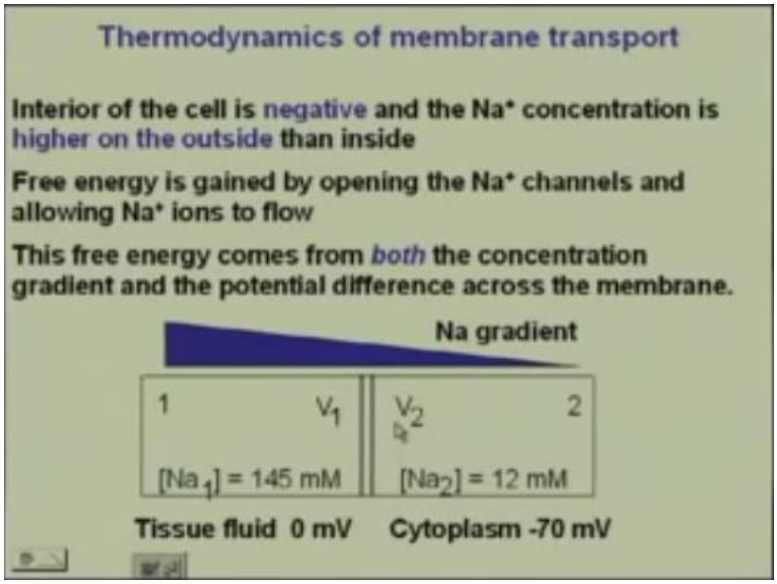

Okay. So what do we have? If, we consider now our sodium gradient, what did we had? We had a 145 millimolar whereas it is outside now 145 millimolar we know that inside of the cell has high potassium and low sodium. So the sodium gradient is such that you are going from the outside to the inside of the cell. So the tissue fluid has 0 millivolts, the cytoplasm has -17, now where as the -17 come from? It is come because of the ion concentrations being different on either side of the membrane.

So the interior of the cell is negative and the sodium concentration is higher on the outside than the inside. The Free energy is gained by opening the sodium channels and allowing the sodium ions to flow. Why? Because we your concentration on the other side is low. So if you are going from a high concentration to a low concentration, then that is favorable, right? We calculated that the Delta Mu is going to be negative for such a case.

Because the ln is going to be negative, right? So we gain free energy by opening the sodium channels and allowing the sodium ions to flow. But we know that the free energy comes from both the concentration gradient and the potential difference across the membrane. And there as I mentioned when we have an H+ case, we are going to have in addition to this, we are going to have a PH gradient as well as that has to be considered in our calculations for Delta G.

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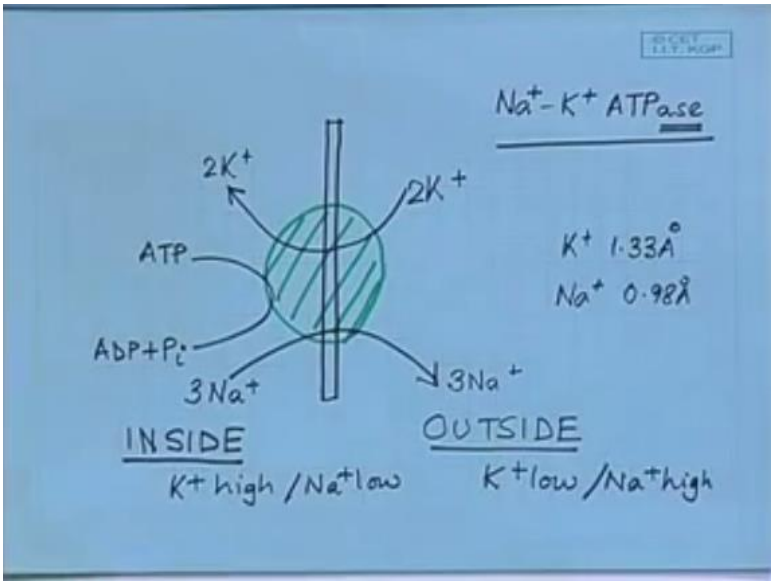

Now what happens is as I was mentioning, the sodium and the potassium sets are actually couple together.

So what we have is that this is our membrane, we have what is called a sodium Na+-K+ it acts so much like an enzyme that is given a name Na+-K+ APTase. Okay. This -ase suffix is usually use for an enzyme. But this sodium potassium pump act so efficiently that, this is been given this name. So say this is occupying this region here. This is where our Na+-K+ ATPase is, okay. What happens is, if this is the outside and this is the inside what happens here, there is a certain gated channel here where we have –

Okay and we have ATP hydrolysis because this has to be driven, it is an ATPase pump so we have ADP, we will be studying all these when we do bioenergetics in more details. Okay, now what has to go from the inside to the outside? Which ion has to go from the inside to the outside?

What do I have higher inside sodium or potassium? Potassium is high inside, and potassium is low outside and the opposite for sodium. So Na+ is low inside and Na+ is high outside.

So whatever is going out is Na+ from the inside to the outside. And what is coming in, is K+. Okay. Now what happens is, the carrier protein is such or the way it works is such that it takes out three sodium ions and brings in two potassium ions for every cycle that it goes through. Because it is built in such a manner, you understand that the K+ ions are larger in size. What is the size? The K+ is about 1.33 Angstroms and the Na+ is 0.98 Angstrom. Okay.

So three of these Na+ are bought from the inside to the outside and two of the K+ are taken from the outside to the inside, and then what happens is this is then ready to take the sodium outside again, Okay, because you have to get back to where it started from, just like an enzymatic reaction. So let us see how this works. Okay.

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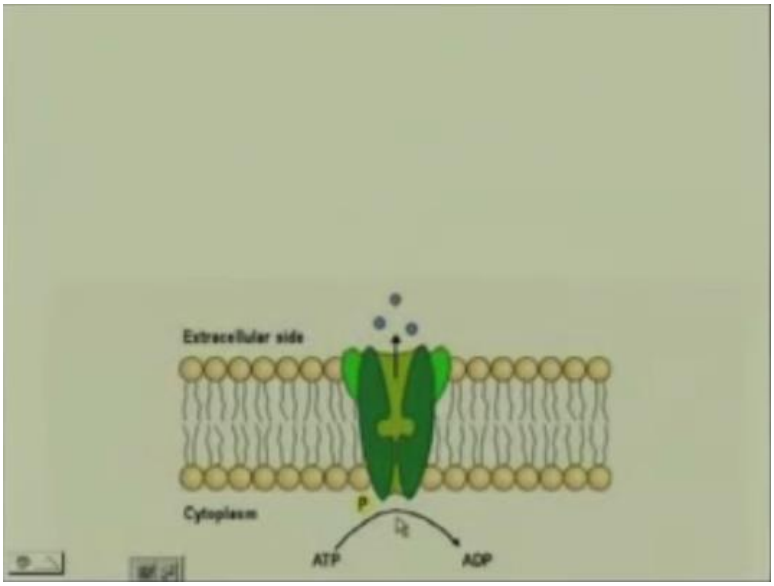

Now what happens is we have the Extracellular side, what do you mean by the extracellular side, the outside. And we have the cytoplasm. What is a cytoplasm? It is a cell matrix inside the cell. Now what is going to happen is.

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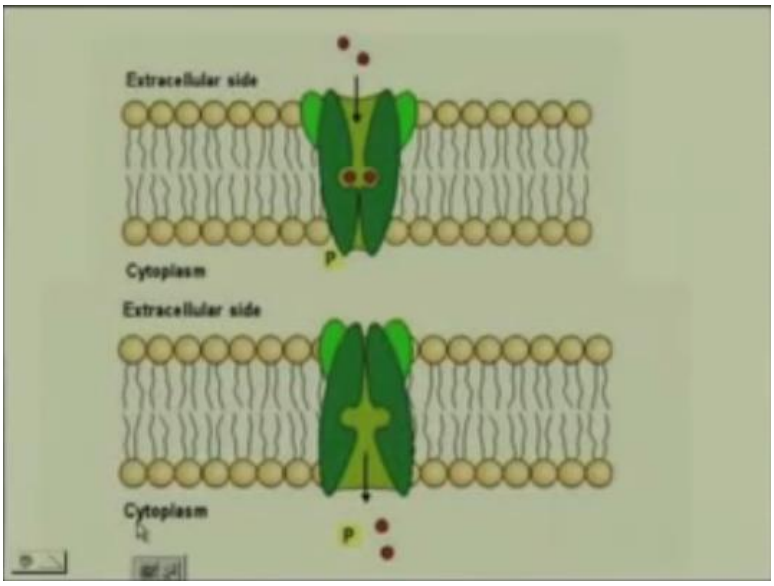

So what we have here is the cytoplasm and the extracellular side. These are the three sodium ions. So where is a sodium ions, where are the sodium ions going? They are going from the cytoplasm they have to be taken outside because we don't need a large amount of sodium ions inside the cell. So what is going to happen, is these three sodium ions get embedded in this protein, okay this carrier and they fit in quiet some (()) (43:23) this point.

So these three sodium ions have come from where, they have come from the inside of the cell, they are bound here and they have to be pushed outside. Now once the sodium ions bound or they sit in here that is a conformational change that occurs and we have ATP go to ADP releasing a phosphate. So what do we have? We have an energetic procedure that has to occur here that is going to release the three sodium ions to the outside of the cell.

Now to have this protein back to where it is, it has to come back to this conformation. Okay it is now an open conformation; it has released the sodium ions that were bound to it. So in the next step what happens, is from the extracellular side it takes up to potassium. Okay. So the two potassium then sit in this side in the protein and bring about such a conformational change that this potassium ions are released on the cytoplasmic side.

Okay, just like you would expect to happen because you want this level the K+ level to be high inside and the K+ level to be low, where? Outside. Okay, now this is ensured by, let us look at

the previous one, what happens here is we have these three sodium ions, the three sodium ions came in from the cytoplasmic side and were released on the extracellular side on the outside of the cell. But to get the conformational aspect of the protein back to where it started from, so it can accept another set of three sodium ions.

What is going to happen? It has to get back to the same conformation. Okay. Because what happens in this carrier protein is you have a conformational change that occurs. And in this conformational change you have to get it back to the original conformation so that it can perform the procedure once more because it has to keep on doing this, there has to constantly do this. So we have the three sodium ions that go through and they are released on the extracellular side.

Then you have the potassium ions that bind to the protein that are eliminator on the cytoplasmic side to maintain this.

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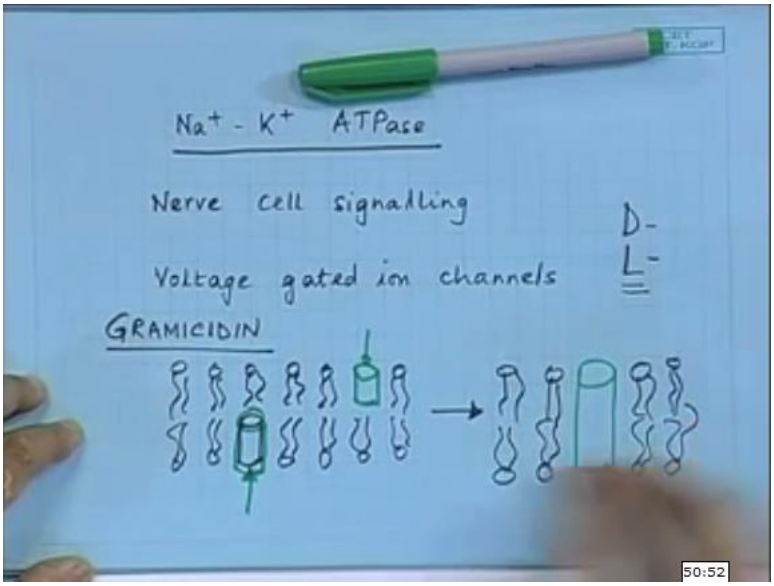

Now this is extremely important, this Na+- K+ ATPase pump as it is called, which is also known as a sodium-potassium pump. Okay, it is also known as a sodium-potassium pump. Now what we have, this is extremely important in Nerve Cell Signaling which is why if you have an imbalance your brain gets affected and you have what is called confusion. Okay. You do not remember things because of the imbalance of sodium-potassium.

You have an – you do not have proper cell signaling which affects your brain. Okay. Then what you have in these cases is what are called Voltage gated ion channels. So in these voltage gated ion channels what do we have? We have – when we have our lipid membrane, for example in gramicidin what happens is, you have a say a single channel for gramicidin, initially it has part of the lipid membrane.

Let us just out the gramicidin in a different color. And one of them is here. They have poirs halfway through the membrane. Okay something like that. Now what happens is when it has to form an ion channel what is the moment that can occur for these lipid membranes. You have lateral diffusion and you have Flip-Flop as well, okay. Now when lateral diffusion occurs in this case, what happens is at one point there is a dimer formation.

What happens is this channel, this is your gramicidin half and this is a gramicidin monomer. This is another monomer. Now, when there is lateral diffusion at one point what happens is it forms the channel through and through. And then because, what is going to happen is even though an ion may get in here, it will not get to the other side because the lipid hydrophobic tail is there. Okay.

The same thing for this case. An ion can come from whichever way you are talking about inside or outside, extracellular, intercellular. An ion can get through that it will not come to the other side because there is no channel through it. But, due to the lateral diffusion at one point what is going to happen is you are going to get a channel. This is what you see when you form gramicidin.

Okay, this is what a gramicidin and gramicidin is unique in that has I mentioned the amino acids in apart from D it has apart from L amino acid which are common it has D amino acids is well. Okay. So that happens in this case? You have the monomers that are present and it forms a dimer. What happens in this case then? You have an ion channel that will allow the flux of ion through and through. Okay. And why is this possible? It is possible because your whole membrane is fluid in nature.

Okay because of the fluidity, because of the lateral moment, it is possible that you have these ion channels that allow the transfer of ions inside and outside. So what we have studied today, is membrane transport, okay. Basically what we understand is that for the membrane transport to occur we have concentration gradient, okay. We have specific types of transport; active transport that requires energy, passive transport that is just going to allow the permeability of the molecules to solute molecules through and through.

And we have specific molecules that have to be have specific concentrations inside and outside the cell as a result of which there is going to be a potential developed because of the charged species that have to be transfer and we have the concentration gradient as well. And we went on to do some free energy thermodynamics, the thermodynamic of membrane transport where we calculate what the free energy changes work, okay. Thank you.